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[Title of the Invention] BODY FAT COMBUSTION PROMOTER

[Abstract]

[Object] A body fat combustion promoter comprising, as an active ingredient, an oil or fat containing 5% by weight or more of diglyceride and/or monoglyceride each containing 15% by weight or more of  $\omega$ 3-based unsaturated acyl groups in constituent acyl groups.

[Effect] When the body fat combustion promoter of the present invention is used, body fat is remarkably reduced safely and efficiently with a small amount reasonably without changing the eating habits, and visceral fat, and blood neutral fat are remarkably reduced, and also liver fat is reduced and a liver function is also improved.

[Claims]

[Claim 1] A body fat combustion promoter comprising, as an active ingredient, an oil or fat containing 5% by weight or more of diglyceride and/or monoglyceride each containing 15% by weight or more of  $\omega$ 3-based unsaturated acyl groups in constituent acyl groups.

[Detailed Description of the Invention]

[0001]

[Technical field of the Invention] The present invention relates to a body fat combustion promoter which is excellent in the effect of reducing body fat, visceral fat and liver fat and is also safe.

[0002]

[Prior Art] With recent progress of the study on a relation between distribution of body fat and various geriatric diseases, it is proposed that accumulation of visceral fat such as intraabdominal fat, liver fat or the like has a close correlation with not only obesity, but also diabetes, hyperlipemia, liver disease and hypertension. Therefore, it is important to reduce body fat so as to prevent and treat these diseases.

[0003] Exercise and meal are important so as to reduce the body fat, but control of exercise and meal is often accompanied by difficulty. Although a trial of reducing body fat by drug therapy is made, a drug to be used is

insufficient in safety.

[0004]

[Problems to be Solved by the Invention] An object of the present invention is to provide a body fat combustion promoter which is safe and also exerts high body fat reducing effect.

[0005]

[Means for Solving the Problems] The present inventors have intensively studied taking notice of the content of a diglyceride and a monoglyceride in an oil or fat and the content of  $\omega$ 3-based unsaturated acyl groups in constituent acyl groups, and found that an oil or fat containing a specific amount of them has excellent body fat combustion promoting effect.

[0006] That is, the present invention provides a body fat combustion promoter comprising, as an active ingredient, an oil or fat containing 5% by weight or more of diglyceride and/or monoglyceride each containing 15% by weight or more of  $\omega$ 3-based unsaturated acyl groups in constituent acyl groups.

[0007]

[Embodiments] The oil or fat used in the body fat combustion promoter of the present invention contains diglyceride and/or monoglyceride in the amount of 5% by weight (hereinafter merely expressed by %) or more,

preferably 15% or more, still more preferably 40% or more, and particularly preferably 50% or more. When the content of diglyceride and/or monoglyceride is less than 5%, sufficient body fat reducing effect cannot be obtained.

[0008] The content of  $\omega$ 3-based unsaturated acyl groups in constituent acyl groups in diglyceride and/or monoglyceride contained in the oil or fat used in the present invention must be 15% or more, preferably 20% or more, and particularly preferably 25% or more, in view of the body fat reducing effect. The  $\omega$ 3-based unsaturated acyl groups as used herein mean acyl groups in which a first unsaturated bond is located on a third carbon atom from the  $\omega$ -position when the position of a carbon-carbon unsaturated bond is specified by the  $\omega$ -position, said acyl groups having two or more carbon-carbon unsaturated bonds. Acyl groups having 3 to 6 carbon-carbon unsaturated bonds are preferred. The  $\omega$ 3-based unsaturated acyl groups having 20 or more carbon atoms are preferably eicosapentaenoyl, docosapentaenoyl and docosaheptaenoyl groups. The  $\omega$ 3-based unsaturated acyl groups having less than 20 carbon atoms are preferably  $\alpha$ -linoleyl groups (all cis-9,12,15-octadecatrienoyl groups). Those having 20 or more carbon atoms have high body fat reducing effect and are particularly excellent in liver fat reducing effect and liver function improving effect. Antitumor and antiallergic

effects based on  $\omega$ 3 fatty acid can be expected. Those having less than 20 carbon atoms also have body fat reducing effect and have excellent oxidation stability and good flavor, and are therefore suited for applications which require excellent oxidation stability and good flavor.

[0009] The oil or fat used in the present invention preferably contains, in addition to the above-described diglyceride and monoglyceride, triglyceride in the amount of 0.1 to 95%, more preferably 0.1 to 85%, still more preferably 0.1 to 60%, and particularly preferably 0.1 to 50%. The number of carbon atoms of acyl groups constituting the diglyceride and/or monoglyceride is not particularly limited, and is from 8 to 24, and particularly preferably from 16 to 22. The amount of the unsaturated acyl groups is preferably 55% or more, more preferably 70% or more, and particularly preferably 90% or more, based on the total acyl groups. The composition of acyl groups constituting the triglyceride contained in the oil or fat used in the present invention is preferably the same as that of acyl groups of the above diglyceride and monoglyceride.

[0010] Particularly preferred composition of the oil or fat used in the present invention is shown. Regarding the diglyceride and/or monoglyceride, in view of decrease in viscosity and oxidation stability, the content of the  $\omega$ 3-

based unsaturated acyl groups is preferably 15% or more, more preferably from 20 to 70%, and particularly preferably from 25 to 65%. The content of the monoene acyl groups is preferably from 10 to 85%, more preferably from 12 to 45%, and particularly preferably from 14 to 35%. The monoene acyl groups are acyl groups having one carbon-carbon double bond and are preferably exadecamonoenoyl, octadecamonoenoyl, eicosadecamonoenoyl and docosadecamonoenoyl groups.

[0011] It is preferred that the constituent acyl groups of the diglyceride and monoglyceride further contain  $\omega$ 6-based unsaturated acyl groups. The  $\omega$ 6-based unsaturated acyl groups as used herein mean acyl groups in which a first unsaturated bond is located on a sixth carbon atom from the  $\omega$ -position when the position of a carbon-carbon unsaturated bond is specified by the  $\omega$ -position, said acyl groups having two or more carbon-carbon unsaturated bonds. The number of the carbon-carbon unsaturated bond is preferably from 3 to 6. When the constituent acyl groups have  $\omega$ 6-based unsaturated acyl groups, the antagonism suppresses side effects such as hemolysis and hemorrhage exerted by excess introduction of  $\omega$ 3-based unsaturated acyl groups, and thus promoting exhibition of bioactivity of  $\omega$ 3-based unsaturated acyl groups. Examples of the  $\omega$ 6-based unsaturated acyl groups include linoleyl groups (cis,cis-9,12-octadecadienoyl groups),  $\gamma$ -linolenoyl groups (all cis-

6,9,12-octadecatrienoyl groups) and arachidoyl groups (all cis-5,8,11,14-eicosatetraenoyl groups), and are preferably linoleyl groups. The content of the 6-based unsaturated acyl groups in the acyl groups constituting diglyceride and/or monoglyceride is preferably from 0.5 to 75%, more preferably from 0.5 to 50%, and particularly preferably from 1 to 25%, in view of exertion of more remarkable effect.

[0012] The oil or fat used in the present invention may contain a glyceride polymer so as to improve oxidation stability. The glyceride polymer is a polymer in which glycerides such as triglyceride, diglyceride and monoglyceride are polymerized the molecules (for example, Chemistry and Creature, Vol. 21, page 179, 1983) and there is no particular limitation on the polymerization degree of the glyceride and the position of the fatty acid ester. The content of the glyceride polymer in the oil or fat is preferably from 0.1 to 10%, more preferably from 0.2 to 5%, and particularly preferably from 0.3 to 4%, in view of an improvement in oxidation stability of an oil or fat composition and flavor. The amount of the glyceride polymer can be adjusted by appropriately adjusting the reaction temperature conditions upon synthesis of the glyceride. The glyceride polymer can be determined by the HPLC method using a connected gel filtration chromatography

column. The content of a free fatty acid in the oil or fat is preferably 5% or less.

[0013] The oil or fat used in the present invention can be prepared, for example, by fractionating triglyceride, diglyceride, monoglyceride obtained by an ester exchange reaction of an oil or fat containing  $\omega$ 3-based unsaturated acyl groups as constituent acyl groups, such as fish oil or rape seed oil with glycerin, and appropriately mixing them.

[0014] The oil or fat thus obtained has excellent body fat combustion promoting effect and exhibits excellent bioactivities such as body fat reduction, visceral fat reduction, blood neutral fat reduction, liver fat reduction and improvement in a liver function, and also has high safety. Therefore, the body fat combustion promoter of the present invention can be used as pharmaceuticals and foods. DG and MG in the present invention can be properly used according to applications. When a weight ratio  $DG/(DG + MG)$  is 0.5 or more, the body fat combustion promoter is suited for applications which require oil solubility. In contrast, when the weight ratio is less than 0.5, the body fat combustion promoter is suited for applications which required water solubility.

[0015] When the body fat combustion promoter of the present invention is used as pharmaceuticals, the dosage form includes oral, enteral and intravenous administrations,



and pharmaceuticals for oral administration are preferred. Specific examples of the dosage form include solid preparations such as powders, granules, capsules, pills and tablets; and liquid preparations such as solutions, suspensions and emulsions. These pharmaceuticals for oral administration can be prepared by adding, in addition to the above oil or fat, excipients, disintegrator, binders, lubricants, surfactants, alcohols, water, water soluble polymers, sweeteners, corrigents and sour agents which are usually used according to the form of pharmaceuticals for oral administration using a conventional method. The content of the oil or fat in the pharmaceuticals for oral administration is preferably from 0.1 to 100%, and particularly preferably from 1 to 80%. The pharmaceuticals for oral administration are preferably administered once or dividedly several times in a dose of 0.1 to 50 g per day in terms of the oil or fat.

[0016] Examples of foods include health foods which enable health promotion by a body fat combustion promoting function, functional foods, and specially designated health foods. Specific examples thereof include tablets, granules, dressings such as French dressing, mayonnaises, creams, confectioneries such as chocolates and potato chips, and beverages, which contain the oil or fat. These foods can be prepared by adding, in addition to the oil or fat, food

materials which are usually used according to the kind of foods using a conventional method. The content of the oil or fat in foods varies depending on the kind of food, and is preferably from 0.1 to 100%, and particularly preferably from 1 to 80%. The oil or fat can also be used as food materials, for example, a frying oil used for tempura and fried foods, or a stir-dry oil.

[0017]

[Examples] Preparation Example 1

200 parts by weight of a fish oil (manufactured by Kao Corporation) and 8 parts by weight of glycerin (manufactured by Wako Pure Chemical Industries, Ltd.) were mixed and mixed with 0.6 part by weight of an alkali catalyst (sodium methoxide  $\text{CH}_3\text{ONa}$ ), and then the mixture was subjected to an ester exchange reaction under reduced pressure (0.133 kPa) at 100°C for 4 hours. The resulting reaction product was fractionated by silica gel chromatography and then mixed with 56.1 parts by weight of triglyceride, 42.9 parts by weight of diglyceride and 1.0 part by weight of monoglyceride to prepare an oil or fat 1.

[0018] Preparation Example 2

200 parts by weight of a DHA-rich oil, ("DHA-45" manufactured by Maruha Corporation) and 10 parts by weight of glycerin were mixed, and then the ester exchange reaction and fractionation of each component were carried

out in the same manner as in Preparation Example 1. Then, the resulting fractions were mixed with 10.3 parts by weight of triglyceride, 87.4 parts by weight of diglyceride, 1.9 parts by weight of monoglyceride and 0.4 part by weight of glyceride polymer to prepare an oil or fat 2.

[0019] Preparation Example 3

180 parts by weight of a linseed oil ("Scan Oil", imported by NIHON SHOJI CO., LTD.) and 12 parts by weight of glycerin were mixed, and then the ester exchange reaction and fractionation of each component were carried out in the same manner as in Preparation Example 1. Then, the resulting fractions were mixed with 36.8 parts by weight of triglyceride, 61.3 parts by weight of diglyceride, 0.5 part by weight of monoglyceride, 0.8 part by weight of free fatty acid and 0.6 part by weight of glyceride polymer to prepare an oil or fat 3.

[0020] Preparation Example 4

180 parts by weight of a Perilla ocimoides oil (manufactured by Ohta Oil Mill Co., Ltd.) and 15 parts by weight of glycerin were mixed, and then the ester exchange reaction and fractionation of each component were carried out in the same manner as in Preparation Example 1. Then, the resulting fractions were mixed with 13.3 parts by weight of triglyceride, 24.1 parts by weight of diglyceride, 58.3 parts by weight of monoglyceride, 3.1 parts by weight

of free fatty acid and 1.2 parts by weight of glyceride polymer to prepare an oil or fat 4.

[0021] Preparation Example 5

140 parts by weight of a *Perilla ocimoides* oil, 70 parts by weight of an olive oil (manufactured by Wako Pure Chemical Industries, Ltd.) and 20 parts by weight of glycerin were mixed, and then the ester exchange reaction and fractionation of each component were carried out in the same manner as in Preparation Example 1. Then, a 100% monoglyceride fraction was taken as an oil or fat 5.

[0022] Comparative Example 1, 2

A rape seed oil (manufactured by Nissei Seiyu Co., Ltd.) and a fish oil were respectively taken as an oil or fat 6 (Comparative Example 1) and an oil or fat 7 (Comparative Example 2).

[0023] Comparative Example 3

Among the fraction components obtained in Preparation Example 2, 96.2 parts by weight of triglyceride and 3.8 parts by weight of diglyceride were mixed to prepare an oil or fat 8.

[0024] Comparative Example 4

200 parts by weight of a rape seed oil and 10 parts by weight of glycerin were mixed, and then the ester exchange reaction and fractionation of each component were carried out in the same manner as in Preparation Example 1.

Then, the resulting fractions were mixed with 21.7 parts by weight of triglyceride, 76.5 parts by weight of diglyceride, 1.3 parts by weight of monoglyceride and 0.5 part by weight of free fatty acid to prepare an oil or fat 9.

[0025] Comparative Example 5

200 parts by weight of an olive oil and 20 parts by weight of glycerin were mixed, and then the ester exchange reaction and fractionation of each component were carried out in the same manner as in Preparation Example 1. Then, the resulting fractions were mixed with 0.1 parts by weight of triglyceride, 0.2 part by weight of diglyceride, 99.2 parts by weight of monoglyceride and 0.5 part by weight of free fatty acid to prepare an oil or fat 10.

[0026] Main composition of fatty acids of the diglyceride fraction derived from each oil or fat obtained in Preparation Examples 1 to 5 and Comparative Examples 3, 4 and 5 is shown in Table 1.

[0027] [Table 1]

		Examples					Comparative Examples		
		1	2	3	4	5	3	4	5
$\omega$ 3	C18:3	0	0	60.6	63.1	41.3	0	10.3	0.4
	C20:5	15.2	6.7	0	0	0	6.7	0	0
	C22:6	8.4	46.3	0	0	0	41.3	0	0
Monoene	C16:1	9.1	3.4	0	0	0.2	3.3	0	0.6
	C18:1	4.3	10.5	14.5	14.6	32.5	10.8	49.8	73.8
	C20:1	5.5	1.4	0	0.2	0.4	1.8	0	0
	C22:1	5.2	1.1	0	0.1	0	1.2	0	0
$\omega$ 6	C18:2	2.0	1.3	15.4	14.2	12.9	1.6	29.1	11.1
	C18:3	1.3	0.7	0	0	0	0.5	0	0
Saturated	C14:0	5.8	2.2	0	0	0	2.3	0	0
	C16:0	16.9	11.3	6.6	5.4	6.9	12.5	8.1	9.8
	C18:0	3.5	2.7	2.9	1.5	2.2	3.5	2.7	3.2

Measured by gas chromatography after methylation

[0028] Test Example 1

Male Wistar rats (aged 10 weeks) were divided into 11 groups (each 8 rats) and each diet according to the formulation shown in Table 2 was fed for 2 weeks. After fastening of rats for 18 hours, blood was collected from ventral aorta under ether anesthesia so as to carry out a biochemical test of blood. Simultaneously, fat tissues surrounding liver and kidney were extracted and the weight was measured. The fat tissues (0.5 g) were ground in 10 mL of a chloroform-methanol mixed solution (2:1) using a glass homogenizer and then subjected to suction filtration through a glass fiber filter paper (GA100 47 mm). To the filtrate, physiological saline was added. After gently mixing, later separation was carried out by centrifugation at 3,000 rpm for 10 minutes and the lower layer was taken out and dried under a nitrogen gas flow. The resulting solid body was redissolved in n-hexane (q.s.) and anhydrous sodium sulfate was added. After dehydration, the solvent was removed again under a nitrogen gas flow, followed by drying. The solid body thus obtained was dissolved in 5 mL of 2-propanol to obtain a test solution for determination of lipids. Percent of body fat was measured by a body fat measuring apparatus for small animal (EM-SCAN SA-2, Central Scientific Commerce, Inc.). The amount of triglyceride in blood and fat tissues surrounding liver and kidney was

measured by Triglyceride Test Wako (manufactured by Wako Pure Chemical Industries, Ltd.). Liver total cholesterol amount was measured by Cholesterol E Test Wako (manufactured by Wako Pure Chemical Industries, Ltd.). GOT (glutamic-oxaloacetic transaminase) activity and GPT (glutamic-pyruvic transaminase) activity in blood were measured by the Karmen method (J. Clin. Invest. Vo. 34, page 131, 1955) using aspartic acid and alanine as a substrate after separation of serum. The results are shown in Table 3.

[0029]

[Table 2]

<Formulation of diet>

	Control	Test group (%) 1-10
Casein	20	20
Corn oil	10	10
Oil or fat	0	3* <sup>1</sup>
Mixed with mineral	4	4
Mixed with vitamin	1	1
Cellulose	4	4
Choline chloride	0.15	0.15
Starch	60.85	57.85

\*1: Kind of oil or fat is described in Table 3

[0030]

[Table 3]

Control	Results (relative value), Control = 100		Percent of body fat	Liver TG amount	Amount of TG surrounding kidney	Blood TG amount	GOT	GPT	Liver total cholesterol amount
	10% Corn oil	Comparative Example							
1	Corn oil + Oil or Fat 6	Comparative Example	100	100	100	100	100	100	100
2	Corn oil + Oil or Fat 7	Comparative Example	123	153	128	156	144	110	110
3	Corn oil + Oil or Fat 8	Comparative Example	99	95	100	93	90	103	103
4	Corn oil + Oil or Fat 9	Comparative Example	97	87	98	88	86	99	99
5	Corn oil + Oil or Fat 10	Comparative Example	101	118	115	127	116	105	105
6	Corn oil + Oil or Fat 1	Example	102	110	95	130	121	108	108
7	Corn oil + Oil or Fat 2	Example	88	68	81	75	72	90	90
8	Corn oil + Oil or Fat 3	Example	78	31	66	61	56	85	85
9	Corn oil + Oil or Fat 4	Example	85	60	75	70	64	92	92
10	Corn oil + Oil or Fat 5	Example	83	55	75	68	59	93	93
			86	63	80	72	67	95	95



[0031]

As is apparent from the results shown in Table 3, in the group of rats ingested a diet comprising 10% of a corn oil 10% and 3% of an oil or fat containing 5% or more of diglyceride and/or monoglyceride each having fixed  $\omega$ 3-unsaturated acyl groups, excellent body fat reducing effect is obtained, and an amount of triglyceride surrounding kidney, an liver triglyceride amount, a total liver cholesterol amount, a serum transamylase value (GOT, GPT) and a blood neutral fat amount (TG) are reduced.

[0032] Test Example 2

Three healthy males of aged 32 to 37 (A, B and C) were allowed to digest an oil or fat 2 filled in a soft capsule in a dose of 1 g per day for 6 weeks without varying the eating habits and then Body Mass Index (BMI) ( $\text{weight (kg)} / (\text{height (m)} \times \text{height (m)})$ ), percent of body fat and waist size were measured. The results are shown in Table 4.

[0033]

[Table 4]

		0W	6W
A (Aged 37)	BMI	25.1	24.8
	Percent of body fat (%)	25.3	24.5
	Waist (cm)	87.4	86.1
B (Aged 35)	BMI	23.6	22.9
	Percent of body fat (%)	24.0	23.4
	Waist (cm)	85.5	84.7
C (Aged 32)	BMI	24.2	23.5
	Percent of body fat (%)	24.8	24.1
	Waist (cm)	88.1	86.3

[0034]

As is apparent from the results shown in Table 4, digestion of the body fat combustion promoter of the present invention reduces percentage of body fat without varying the eating habits, and thus BMI and waist size decrease.

[0035] Example 1

[0036]

[Table 5]

Parts by weight

Weak flour	250
Hard flour	250
Very-refined sugar	150
Whole egg	125
Oil or Fat 1 or Oil or Fat 5	100
Shortening (Kao Corporation)	60
Salad oil (Nisshin Seiyu)	40
Salt	2.5

[0037]

Very-refined sugar, salt, an oil or fat 1 or an oil or fat 5, a salad oil and shortening were placed in a bowl, followed by stirring using a Hobert mixer. To the mixture, whole egg was gradually added, followed by stirring using a Hobert mixer. A preliminary prepared mixture of weak flour and hard flour was added dividedly three times, followed by stirring using a Hobert mixer. The dough thus prepared was divided into pieces (25 g) and then filled in a metal mold. After baking in an oven at 160°C for 50 minutes, removal of the mold and further air-cooling, shortbread was prepared.

[0038] Example 2

A soft capsule film (oval type, weight: 150 mg) was filled with 300 mg of an oil or fat 2 or an oil or fat 4 by a conventional method to prepare a soft capsule.

[0039]

[Table 6]

Parts by weight	
Gelatin	70.0
Glycerin	22.9
Methyl paraoxybenzoate	0.15
Propyl paraoxybenzoate	0.15
Purified water	6.8

[0040]

Example 3

[0041]

[Table 7]

Parts by weight	
Egg yolk lecithin	1.2
Glycerin	2.5
Oil or Fat 3	10.0
Purified water	86.3

[0042] Egg yolk lecithin was mixed with glycerin and purified water (2.5 parts) and an oil or fat 3 was gradually added while stirring. To the mixture, purified water (83.8 parts) was gradually added while stirring. The mixed solution was emulsified at 9,000 rpm for 30 minutes by an ultra-homomixer (manufactured by TOKUSYU KIKA KOGYO) and ultrasonic-emulsified (10°C) at 240 W for 30 minutes by

an ultrasonic wave homogenizer (manufactured by Branson), and then the pH was adjusted to 7.4 with an aqueous 0.1 N sodium hydroxide solution). After membrane filter filtration (pore diameter 3  $\mu\text{m}$ , 1.2  $\mu\text{m}$ , 0.45  $\mu\text{m}$ ), dispensing under a nitrogen atmosphere and further sterilization in an autoclave at 121°C for 20 minutes, an intravenous injection was prepared.

[0043]

[Effect of the Invention] When the body fat combustion promoter of the present invention is used, body fat is remarkably reduced safely and efficiently with a small amount reasonably without changing the eating habits, and visceral fat, and blood neutral fat are remarkably reduced, and also liver fat is reduced and a liver function is also improved.

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(54)【発明の名称】 体脂肪燃焼促進剤

(57)【要約】

【課題】 構成アシル基中の $\omega$ 3系不飽和アシル基含量が15重量%以上であるジグリセリド及び/又はモノグリセリドを5重量%以上含有する油脂を有効成分とする体脂肪燃焼促進剤。

【効果】 本発明の体脂肪燃焼促進剤を用いれば、食生活を変えることなく、無理なく少量で、安全に効率よく体脂肪が顕著に低下し、内臓脂肪、血中中性脂肪が著しく減少し、更に肝臓脂肪も低下し、肝機能も改善される。

## 【特許請求の範囲】

【請求項1】 構成アシル基中の $\omega$ 3系不飽和アシル基含量が15重量%以上であるジグリセリド及び／又はモノグリセリドを5重量%以上含有する油脂を有効成分とする体脂肪燃焼促進剤。

## 【発明の詳細な説明】

## 【0001】

【発明の属する技術分野】本発明は体脂肪や内臓脂肪、肝臓脂肪の低下効果に優れ、かつ安全な体脂肪燃焼促進剤に関する。

## 【0002】

【従来の技術】近年、体脂肪の分布と種々の成人病との関係について研究が進み、特に腹腔内脂肪や肝臓脂肪等の内臓脂肪の蓄積は、肥満だけでなく、糖尿病、高脂血症、肝疾患、高血圧症などと高い相関関係があることが示されている。従って体脂肪を低下させることは、これらの疾患を予防及び治療するうえで重要である。

【0003】当該体脂肪を低下させるには、運動及び食事が重要であるが、管理に困難を伴うことが多い。一方、薬物療法により体脂肪を低下させようとする試みもあるが、用いる薬物の安全性が問題となる。

## 【0004】

【発明が解決しようとする課題】本発明の目的は安全でかつ体脂肪低下効果の高い体脂肪燃焼促進剤を提供することにある。

## 【0005】

【課題を解決するための手段】本発明者らは油脂中のジグリセリド及びモノグリセリドの含量とそれらの構成アシル基中の $\omega$ 3系不飽和アシル基含量に着目して検討したところ、これらを、特定量含む油脂に優れた体脂肪燃焼促進作用があることを見出した。

【0006】すなわち、本発明は、構成脂肪酸中の $\omega$ 3系不飽和アシル基含量が15重量%以上であるジグリセリド及び／又はモノグリセリドを5重量%以上含有する油脂を有効成分とする体脂肪燃焼促進剤を提供するものである。

## 【0007】

【発明の実施の形態】本発明の体脂肪燃焼促進剤に用いられる油脂は、ジグリセリド及び／又はモノグリセリドを5重量%（以下、単に%で示す）以上含有するものであり、好ましくは15%以上、更に好ましくは40%以上、特に好ましくは50%以上含有するものである。ジグリセリド及び／又はモノグリセリド含量が5%未満では充分な体脂肪低下効果を得ることができない。

【0008】本発明に用いられる油脂に含まれるジグリセリド及び／又はモノグリセリドの構成アシル基中の $\omega$ 3系不飽和アシル基含量は、体脂肪低下効果の点から15%以上が必要であり、好ましくは20%以上、特に好ましくは25%以上である。ここで上記 $\omega$ 3系不飽和アシル基とは炭素-炭素不飽和結合の位置を $\omega$ 位から特定

し、 $\omega$ 位から3番目の炭素原子に最初の不飽和結合が位置するアシル基であって、かつ炭素-炭素不飽和結合を2以上有するものをいう。炭素-炭素不飽和結合を3〜6有するものが好ましい。炭素数20以上の $\omega$ 3系不飽和アシル基としては、エイコサペンタエノイル基、ドコサペンタエノイル基、ドコサヘキサエノイル基が好ましい。また、炭素数20未満の $\omega$ 3系不飽和アシル基としては、 $\alpha$ -リノレイル基（all cis-9, 12, 15-オクタデカトリエノイル基）が好ましい。炭素数20以上のものは体脂肪低下効果が高いが、特に肝臓脂肪低下、肝機能改善効果に優れている。また $\omega$ 3脂肪酸に基づく抗腫瘍、抗アレルギー効果等が期待できる。炭素数20未満のものも体脂肪低下効果を有するが、特に酸化安定性がよく、風味良好なので、これらが求められる用途に適している。

【0009】また、本発明で用いられる油脂中には、上記ジグリセリド及びモノグリセリド以外に、トリグリセリドを好ましくは0.1〜95%、より好ましくは0.1〜85%、更に好ましくは0.1〜60%、特に好ましくは0.1〜50%含有する。このジグリセリド及び／又はモノグリセリドを構成するアシル基の炭素数に特に制限はないが、8〜24、特に16〜22が好ましい。不飽和アシル基の量は、全アシル基の55%以上が好ましく、70%以上がより好ましく、90%以上が特に好ましい。本発明で用いられる油脂に含まれるトリグリセリドを構成するアシル基の組成も上記ジグリセリド及びモノグリセリドのアシル基組成と同様であることが好ましい。

【0010】以下、本発明に用いる油脂の特に好ましい組成を示す。ジグリセリド及び／又はモノグリセリドは粘度低下及び酸化安定性の観点から、 $\omega$ 3系不飽和アシル基含量が15%以上、更に20〜70%、特に25〜65%であるのが好ましく、またモノエンアシル基含量が10〜85%、更に12〜45%、特に14〜35%であるのが好ましい。ここでモノエンアシル基は、炭素-炭素二重結合を1個有するアシル基であり、ヘキサデカモノエノイル基、オクタデカモノエノイル基、エイコサデカモノエノイル基、ドコサデカモノエノイル基が好ましい。

【0011】ジグリセリド及びモノグリセリドの構成アシル基中は、更に $\omega$ 6系不飽和アシル基を含有するものであることが好ましい。ここで $\omega$ 6系不飽和アシル基とは、炭素-炭素不飽和結合の位置を $\omega$ 位から特定し、 $\omega$ 位から6番目の炭素原子に最初の不飽和結合が位置するアシル基であって、かつ炭素-炭素不飽和結合を2以上有するものをいう。炭素-炭素不飽和結合数は3〜6が好ましい。 $\omega$ 6系不飽和アシル基を含有すれば、その拮抗作用により、 $\omega$ 3系不飽和アシル基を過剰に摂取した際に生じる溶血、出血等の副作用の発現を抑制し、 $\omega$ 3系不飽和アシル基が有する生理活性の発現を容易にする

ことができる。ω6系不飽和アシル基としては、リノレイル基 (cis, cis-9, 12-オクタデカジエノイル基)、γ-リノレノイル基 (All cis-6, 9, 12-オクタデカトリエノイル基、アラキドイル基 (All cis-5, 8, 11, 14-エイコサテトラエノイル基) 等が挙げられるがリノレイル基が好ましい。ω6系不飽和アシル基の、ジグリセリド及び/又はモノグリセリド構成アシル基中の含有量は、上記効果をより顕著とする点から、0.5~75%が好ましく、0.5~50%がより好ましく、1~25%が特に好ましい。

【0012】本発明に用いられる油脂には、酸化安定性を向上させるために、グリセリド重合物を含有してもよい。グリセリド重合物は、トリグリセリド、ジグリセリド、モノグリセリドといったグリセリドが、分子間で重合したもので (例えば、化学と生物21巻179頁1983年)、グリセリドの重合度、脂肪酸エステルの位置等に特に制限はない。グリセリド重合物の油脂中の含有量は、油脂組成物の酸化安定性の向上及び風味の観点から、0.1~10%が好ましく、0.2~5%がより好ましく、0.3~4%が特に好ましい。かかるグリセリド重合物は、グリセリド合成時、反応温度条件等を適宜調整することにより、その量を調整できる。グリセリド重合物はゲル濾過クロマトグラフィーカラムを接続したHPLC法により定量できる。また、油脂中の遊離脂肪酸含有量は5%以下が好ましい。

【0013】本発明に用いられる油脂は、例えば魚油、ナタネ油等のω3系不飽和アシル基等を構成アシル基として含有する油脂とグリセリンとのエステル交換反応等により得られたトリグリセリド、ジグリセリド、モノグリセリド等を分画し、次いでこれらを適宜混合することによって製造することができる。

【0014】かくして得られた油脂は、優れた体脂肪燃焼促進効果を有し、体脂肪低下、内臓脂肪低下、血中中性脂肪消費、肝臓脂肪低下、肝機能改善等の優れた生理活性を示し、また安全性が高い。従って、本発明の体脂肪燃焼促進剤は医薬及び食品として用いることができる。本発明で用いるDGとMGは用途により使いわけることができる。DG/(DG+MG)重量比が0.5以上の場合には油溶性が求められる用途、0.5未満の場合には水溶性が求められる用途に適している。

【0015】本発明体脂肪燃焼促進剤を医薬として用いる場合、投与形態としては経口、経腸及び静脈内投与等が挙げられるが、経口投与用医薬が好ましい。具体的には散剤、顆粒剤、カプセル剤、丸剤、錠剤等の固形製剤、水剤、懸濁剤、乳剤等の液剤等が挙げられる。これらの経口投与剤は、上記油脂の他、経口投与剤の形態に応じて一般に用いられる、賦形剤、崩壊剤、結合剤、滑沢剤、界面活性剤、アルコール類、水、水溶性高分子、甘味料、矯味剤、酸味料等を添加し、常法に従って製造することができる。前記の油脂の経口投与用医薬製剤へ

の配合量は、一般に0.1~100%、特に1~80%が好ましい。また、投与量は、前記油脂として、1日当たり0.1~50gを、1~数回に分けて投与することが好ましい。

【0016】食品としては、例えば体脂肪燃焼促進機能を発揮して健康増進を図る健康食品、機能性食品、特定保健用食品等が挙げられる。具体的には、かかる油脂を配合した錠剤、顆粒剤、フレンチドレッシング等のドレッシング類、マヨネーズ類、クリーム類、チョコレートやポテトチップス等の菓子類、飲料等が挙げられる。かかる食品は、上記油脂の他に、食品の種類に応じて一般に用いられる食品原料を添加し、常法にしたがって製造することができる。上記の油脂の食品への配合量は、食品の種類によっても異なるが、一般に0.1~100%、特に1~80%が好ましい。また天ぷらやフライ等の揚げ物用油、あるいは炒め物用油等の食品素材として用いることができる。

#### 【0017】

##### 【実施例】製造例1

魚油 (花王 (株) 製) 200重量部とグリセリン (和光純薬工業 (株) 製) 8重量部とを混合し、アルカリ触媒 (ナトリウムメトキサイド  $\text{CH}_3\text{ONa}$ ) 0.6重量部を混合し、減圧下 (0.133kPa) 100℃で4時間エステル交換反応を行った。得られた反応生成物を、シリカゲルカラムクロマトグラフィーで分画し、次いでトリグリセリド56.1重量部、ジグリセリド42.9重量部、モノグリセリド1.0重量部を混合して油脂1を製造した。

##### 【0018】製造例2

DHA高含有油 (マルハ (株) 製「DHA-45」) 200重量部とグリセリン10重量部を混合し、製造例1と同様にしてエステル交換反応、各成分の分画を行った。次いでトリグリセリド10.3重量部、ジグリセリド87.4重量部、モノグリセリド1.9重量部及びグリセリド重合物0.4重量部を混合して油脂2を製造した。

##### 【0019】製造例3

亜麻仁油 (「スキャンオイル」、輸入元: 日本商事 (株)) 180重量部とグリセリン12重量部を混合し、製造例1と同様にしてエステル交換反応、各成分分画を行った。次いで、トリグリセリド36.8重量部、ジグリセリド61.3重量部、モノグリセリド0.5重量部、遊離脂肪酸0.8重量部、グリセリド重合物0.6重量部を混合して油脂3を製造した。

##### 【0020】製造例4

エゴマ油 (太田油脂 (株) 製) 180重量部とグリセリン15重量部を混合し、製造例1と同様にしてエステル交換反応、各成分の分画を行った。次いでトリグリセリド13.3重量部、ジグリセリド24.1重量部、モノグリセリド58.3重量部、遊離脂肪酸3.1重量部及

びグリセリド重合物1.2重量部を混合して油脂4を製造した。

#### 【0021】製造例5

エゴマ油140重量部、オリーブ油（和光純薬工業（株）製）70重量部及びグリセリン20重量部を混合し、製造例1と同様にしてエステル交換反応、各成分の分画を行った。次いでモノグリセリド100%画分を油脂5とした。

#### 【0022】比較例1、2

ナタネ油（日清製油（株）製）及び魚油を、それぞれ油脂6（比較例1）及び油脂7（比較例2）とした。

#### 【0023】比較例3

製造例2で得られた各分画成分のうち、トリグリセリド96.2重量部及びジグリセリド3.8重量部を混合して油脂8を製造した。

#### 【0024】比較例4

ナタネ油200重量部とグリセリン10重量部を混合

し、製造例1と同様にしてエステル交換反応、各成分の分画を行った。次いでトリグリセリド21.7重量部、ジグリセリド76.5重量部、モノグリセリド1.3重量部及び遊離脂肪酸0.5重量部を混合して油脂9を製造した。

#### 【0025】比較例5

オリーブ油200重量部とグリセリン20重量部を混合し、製造例1と同様にしてエステル交換反応、各成分の分画を行った。次いでトリグリセリド0.1重量部、ジグリセリド0.2重量部、モノグリセリド99.2重量部、遊離脂肪酸0.5重量部を混合して油脂10を製造した。

【0026】製造例1～5及び比較例3、4及び5で得られた各油脂由来のジグリセリド画分の主要脂肪酸組成を表1に示す。

#### 【0027】

【表1】

		実 施 例					比 較 例		
		1	2	3	4	5	3	4	5
ω 3	C18:3	0	0	60.6	63.1	41.3	0	10.3	0.4
	C20:5	15.2	6.7	0	0	0	6.7	0	0
	C22:6	8.4	46.3	0	0	0	41.3	0	0
モノ エン	C16:1	9.1	3.4	0	0	0.2	3.3	0	0.6
	C18:1	4.3	10.5	14.5	14.6	32.5	10.8	49.8	73.8
	C20:1	5.5	1.4	0	0.2	0.4	1.8	0	0
	C22:1	5.2	1.1	0	0.1	0	1.2	0	0
ω 6	C18:2	2.0	1.3	15.4	14.2	12.9	1.6	29.1	11.1
	C18:3	1.3	0.7	0	0	0	0.5	0	0
飽和	C14:0	5.8	2.2	0	0	0	2.3	0	0
	C16:0	16.9	11.3	6.6	5.4	6.9	12.5	8.1	9.8
	C18:0	3.5	2.7	2.9	1.5	2.2	3.5	2.7	3.2

メチル化後、ガスクロマトグラフィーにて測定

#### 【0028】試験例1

10週齢のWistar系雄性ラットを各群8匹ずつ11群に分け、表2記載の組成の食餌を2週間与えた。その後ラットを18時間絶食させた後、エーテル麻酔下で、血液の生化学試験を行うために腹部大動脈より採血を行った。同時に肝臓、腎臓周囲脂肪組織を摘出して重量を測定した後、その0.5gを10mLクロロフォルム-メタノール混液（2：1）中にて、ガラスホモジナイザーを用いて破碎し、ガラス繊維濾紙（GA100 47mm）で吸引濾過した。濾液に生理食塩水を加えて穏やかに混和した後、遠心分離（3000rpm×10分）を行い分層させ、下層を取り出して窒素気流下で乾固した。得られた固形物を、適量のn-ヘキサンで再溶解し、無水硫酸ナトリウムを加えて脱水した後、再度窒素気流下で溶媒を除去し乾固した。この固形物を、5mLの2-プロパノールに溶解し脂質定量の試験液とした。体脂肪率は小動物用体脂肪測定装置（EM-SCAN SA-2 セントラル科学貿易）で測定した。血中及び肝臓、腎臓周囲脂肪組織のトリグリセリドは、トリグリセリド テ

ストワコー（和光純薬製）にて測定した。肝臓の総コレステロールはコレステロールEテストワコー（和光純薬製）にて測定した。また、血中のGOT（グルタミン酸オキサロ酢酸トランスアミナーゼ）活性、GPT（グルタミン酸ピルビン酸トランスアミナーゼ）活性は、血清を分離後、Karmen法（J. Clin. Invest. 34 巻 131頁 1955 年）にて、それぞれアスパラギン酸、アラニンを基質として測定を行った。得られた結果を表3に示す。

#### 【0029】

【表2】

<食餌組成>

	コントロール	試験群（%）1～10
カゼイン	20	20
コーン油	10	10
油脂	0	3*1
ミネラル混合	4	4
ビタミン混合	1	1
セルロース	4	4
塩化コリン	0.15	0.15
スターチ	60.85	57.85

\*1：油脂の種類は表3に記載。



【0030】

【表3】

結 果 (相対値) コントロール=100			体脂肪率	肝臓TG量	腎臓周囲 TG量	血中TG量	GOT	GPT	肝臓総コレス テロール量
コントロール	コーン油10%	比較例	100	100	100	100	100	100	100
1	コーン油+油脂6	比較例	123	153	109	128	156	144	110
2	コーン油+油脂7	比較例	99	95	101	100	93	90	103
3	コーン油+油脂8	比較例	97	87	100	98	88	86	99
4	コーン油+油脂9	比較例	101	118	104	115	127	116	105
5	コーン油+油脂10	比較例	102	110	104	95	130	121	108
6	コーン油+油脂1	実施例	88	68	95	81	75	72	90
7	コーン油+油脂2	実施例	78	31	84	66	61	56	85
8	コーン油+油脂3	実施例	85	60	94	75	70	64	92
9	コーン油+油脂4	実施例	83	55	93	75	68	59	93
10	コーン油+油脂5	実施例	86	63	89	80	72	67	95

【0031】表3の結果より、コーン油10%に一定のω3不飽和アシル基含量を有するジグリセリド及び／又はモノグリセリドを5%以上含む油脂を3%添加した食餌摂取群では、優れた体脂肪低下効果が得られ、腎周囲トリグリセリド量、肝臓トリグリセリド量、肝臓総コレステロール量、血清トランスアミナーゼ値 (GOT, GPT)、及び血中中性脂肪量 (TG) も低下させることがわかる。

【0032】試験例2

32～37歳の健康男性3名 (A, B, C) に、食生活を変えることなく、ソフトカプセルに充填した油脂2を1日1g6週間摂取させ、BMI (Body Mass Index : 体重kg / (身長m × 身長m))、体脂肪率、ウエストサイズを測定した。結果を表4に示す。

【0033】

【表4】

		0 W	6 W
A 37歳	BMI	25.1	24.8
	体脂肪率 (%)	25.3	24.5
	ウエスト (cm)	87.4	86.1
B 35歳	BMI	23.6	22.9
	体脂肪率 (%)	24.0	23.4
	ウエスト (cm)	85.5	84.7
C 32歳	BMI	24.2	23.5
	体脂肪率 (%)	24.8	24.1
	ウエスト (cm)	88.1	86.3

【0034】表4の結果より、本発明の体脂肪燃焼促進剤を摂取すると、食生活を変えることなく、体脂肪率が減少し、それに伴いBMI、ウエストサイズが低下することがわかる。

【0035】実施例1

【0036】

【表5】

重量部

薄力粉	250
強力粉	250
上白糖	150
全卵	125
油脂1又は油脂5	100
ショートニング (花王)	60
サラダ油 (日清製油)	40
食塩	2.5

【0037】上白糖、食塩、油脂1又は油脂5、サラダ油、ショートニングをボールに入れ、ホバートミキサーにて攪拌した。これに全卵を徐々に加え、ホバートミキサーで攪拌した。予め混合しておいた薄力粉と強力粉を3回に分けて加え、ホバートミキサーで攪拌した。調製した生地を25gずつ小分けし、金属製型枠に詰めた。オープン焼成 (160℃、50分) 後、型枠から外し、放冷してショートブレッド製造した。

【0038】実施例2

下記組成のソフトカプセル皮 (オパール型、重さ150mg) に油脂2又は油脂4を300mg常法により充填し、ソフトカプセルを作製した。

【0039】

【表6】

重量部

ゼラチン	70.0
グリセリン	22.9
パラオキシ安息香酸メチル	0.15
パラオキシ安息香酸プロピル	0.15
精製水	6.8

【0040】実施例3

【0041】

【表7】

重量部	
卵黄レシチン	1.2
グリセリン	2.5
油脂3	10.0
精製水	86.3

【0042】卵黄レシチンにグリセリン、精製水（2.5部）を混合し、更に、油脂3を少量ずつ攪拌しながら加えた。これに精製水（83.8部）を少量ずつ攪拌しながら加えた。ウルトラホモキサー（特殊機化工業社製）を用いて9000rpmで30分間乳化し、超音波ホモジナイザー（ブランソン社製）で、240W30分間

超音波乳化（10℃）し、pHを7.4に調製（0.1N水酸化ナトリウム水溶液）した。次いでメンブランフィルター（孔径3μm、1.2μm、0.45μm）し、窒素雰囲気下で分注後、オートクレーブ滅菌（121℃20分間）して静脈用注射剤を調製した。

#### 【0043】

【発明の効果】本発明の体脂肪燃焼促進剤を用いれば、食生活を変えることなく、無理なく少量で、安全に効率よく体脂肪が顕著に低下し、内臓脂肪、血中中性脂肪が著しく減少し、更に肝臓脂肪も低下し、肝機能も改善される。

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